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A HIGHLY EFFICIENT METHOD FOR INTRODUCTION OF BUTENOLIDE MOIETIES TO VARIOUS ELECTROPHILES

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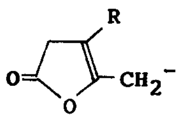
Summary: Lithiated 5-(trimethylsilyl)furfuryl phenyl sulfides or the corresponding diphenylthioacetal can be used efficiently for introduction of butenolide moieties to various types of electrophilic reagents through their addition or substitution reactions followed by oxidation of the silylfuran moieties.

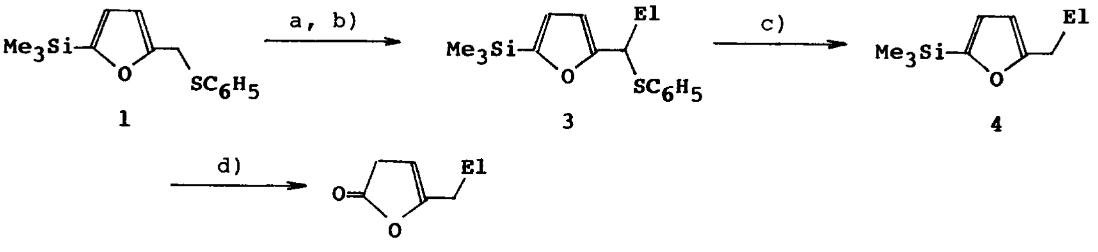
In connection with our synthetic program for hirsutene and its derivatives, it is required to introduce butenolide moiety (**A**) onto 4-position of 2,2-dimethylcyclopentanone. Although such transformations may be performed through conjugate addition of the corresponding nucleophilic species to the cyclopentenone, it is very difficult to manipulate the butenolides themselves as nucleophiles. Here we describe an efficient solution to this transformation on the basis of characteristic features of silylfuran derivative.

In the previous paper, we reported an oxidation reaction of 2-(trimethylsilyl)furans with peracetic acid to the corresponding butenolides.[1] Synthetic utility of this procedure have further been confirmed by other research groups.[2] In addition to this facile oxidative transformation of a silylfuran moiety, use of silylfurfuryl phenyl sulfide **1** or silylfurfural diphenyl dithioacetal **2** has brought about a remarkable progress for our present purpose on the following aspect. It is usually very difficult to handle furfuryl carbanions as nucleophilic reagents because they are quite unstable and undergo a facile ring opening reaction[3] even at low temperature. However, an introduction of a silyl group on 5-position of their furan ring has been found to stabilize such carbanions and to make it very easy to manipulate for several synthetic purposes without any decomposition even at room temperature. Thus, on treating with butyllithium, 5-(trimethylsilyl)furfuryl phenyl sulfide **1** can



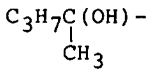
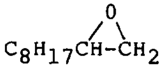
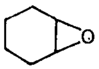
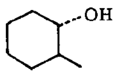
R = H, CH_3

(A)



a) BuLi, b) El^+, c) Raney Ni
d) CH_3CO_3H

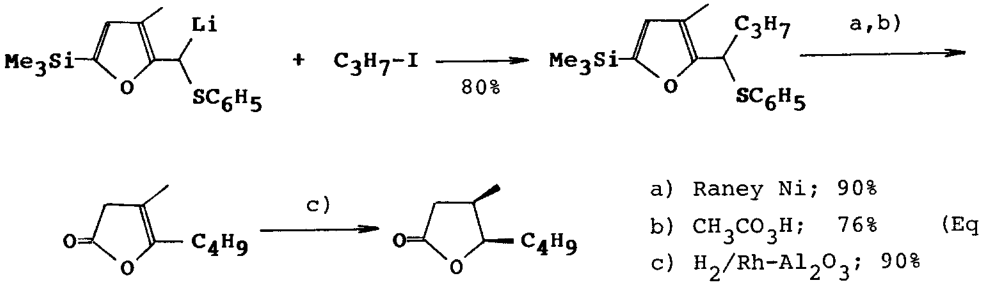
Table. Introduction of Electrophiles and Desulfurization of the Resulting 3.

El^+	El	1 --> 3 (%)	3 --> 4 (%)
$C_5H_{11}Br$	C_5H_{11}	97	100
$(CH_3)_2CHCH_2Br$	$(CH_3)_2CHCH_2-$	92	72
$C_8H_{17}CH{=}O$	$C_8H_{17}CH(OH)-$	89	88
$C_6H_5CH{=}O$	$C_6H_5CH(OH)-$	86	71
$C_3H_7-CO-CH_3$	 $C_3H_7C(OH)(CH_3)-$	84	83
 $C_8H_{17}CH(O)CH_2$	$C_8H_{17}CH(OH)CH_2-$	92	88
		94	--
$C_7H_{15}CO-Cl$	$C_7H_{15}-CO-$	57[a]	--

[a] The reaction was performed in the presence of CuI (1 equiv).

be converted to the corresponding stable anionic species which undergoes alkylation with alkyl halides or oxiranes to afford **3**. In the reaction with aldehydes or ketones, the lithiated phenyl sulfide reacts exclusively on its furfuryl site to yield the corresponding 1,2-addition product **3**.[4] Removal of sulfur group can be effected cleanly by treating with Raney nickel to yield **4**. With some exceptional cases which include an electron-withdrawing substituent, the resulting furan derivatives **4** can be transformed to the butenolides 5 in good yield (65-85%).

The present procedure is applicable for the preparation of 3,4-cis-disubstituted butyrolactones via hydrogenation of **5**. Synthesis of cis-quercus lactone[5] represents a typical example (Eq 2).

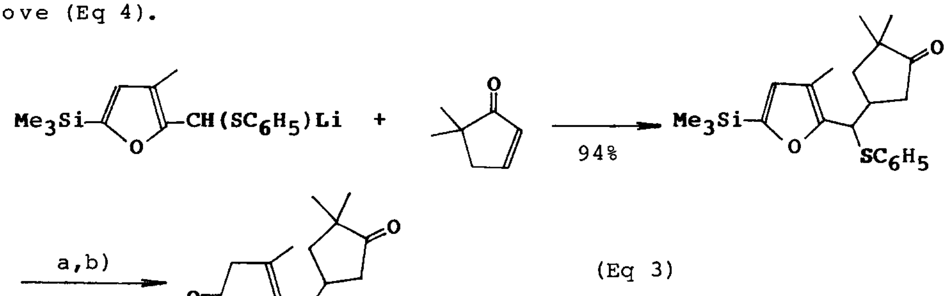


a) Raney Ni; 90%

b) CH_3CO_3H; 76% (Eq 2)

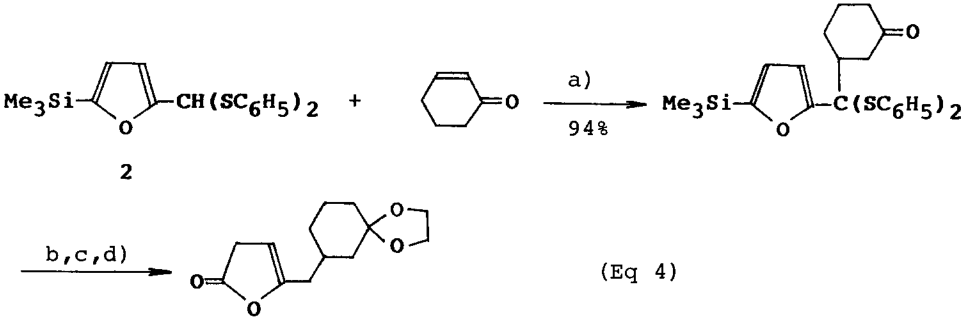
c) $H_2/Rh\text{-}Al_2O_3$; 90%

For synthetic transformations including a conjugate addition of a butenolide moiety, use of the diphenyl dithioacetal 2[6] in place of 1 is much more preferable. Although our initial purpose was successfully attained by using the anionic species of 1 (Eq 3), the reaction with usual enones, e.g. 2-cyclohexenone or its 3-methyl substituted one, leads to the predominant formation of the corresponding 1,2-addition products even in the presence of various Cu(I) salts. In contrast, conjugate addition of lithiated **2** to enones takes place cleanly to afford the 1,4-addition products exclusively. These products were converted to the corresponding butenolides after protection of their ketone functions as acetals followed by removal of the sulfur group and oxidation as above (Eq 4).



(Eq 3)

a) Raney Ni; 93%. b) CH_3CO_3H; 62%



a) BuLi. b) $HO-(CH_2)_2-OH$, $(CO_2H)_2$; 89%. c) Li, $EtNH_2$; 80%. d) CH_3CO_3H; 84%.

Thus, it can be concluded that, in addition to regio-controlled effect on oxidative conversion to butenolide, a 5-trimethylsilyl group on the furan ring plays another important role for stabilization of the furfuryl carbanion, which allows to use the lithiated **1** and **2** as the nucleophilic butenolide equivalent **A**.

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References

1) I. Kuwajima and H. Urabe, Tetrahedron Lett., **22**, 5191 (1981).

2) a) A. G. Schultz and L. A. Motyka, J. Am. Chem. Soc., **104**, 5800 (1982). b) D. Goldsmith, D. Liotta, M. Saindane, L. Waykole, P. Bowen, Tetrahedron Lett., **24**, 5835 (1983). c) S. P. Tanis and D. B. Head, ibid., **25**, 4451 (1984).

3) M. J. Taschner and G. A. Kraus, J. Org. Chem., **43**, 4235 (1978); K. Atsumi and I. Kuwajima, J. Am. Chem. Soc., **101**, 2208 (1979); I. Kuwajima, K. Atsumi, T. Tanaka, and T. Inoue, Chem. Lett., 1239 (1979); I. Kuwajima, S. Hoshino, T. Tanaka, and M. Shimizu, Tetrahedron Lett., **21**, 3209 (1980).

4) In contrast to the phenyl sulfide, the reaction of lithiated ethyl furfuryl sulfide with an aldehyde or a ketone gave a mixture of two regio-isomers arising from addition on its α-position and on the furan ring, respectively.

5) M. Masuda and K. Nishimura, Chem. Lett., 1333 (1981), and references cited therein.

6) The thioacetalization of 5-(trimethylsilyl)furfural was performed with thiophenol in the presence of chlorotrimethylsilane: B. S. Ong and T. H. Chan, Synth. Commun., **7**, 283 (1977).

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